ULTRASOUND STRAIN IMAGING: FROM NANO-SCALE MOTION DETECTION TO MACRO-SCALE FUNCTIONAL IMAGING

C.L. de Korte[1], R.G.P. Lopata[1], M.M. Nillesen[1], G. Weijers[1], N.J. van Hees[3], I.H. Gerrits[1], C. Katsaros[3], L. Kapusta[2], J.M. Thijssen[1],*

[1]Clinical Physics Laboratory and [2]Pediatric Cardiology, Department of Pediatrics,
[3]Department of Orthodontics and Oral Biology
Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands

ABSTRACT

With ultrasound strain imaging, the function of tissue and organs can be identified. The technique uses multiple images, acquired from tissue under different degrees of deformation. We recently applied this technique on hearts and skeletal muscles. Cardiac data was acquired in dogs with a valvar aorta stenosis. Muscle data was acquired from the orbicular oral muscle in the upper lip.

For accurate assessment of deformation, the displacement of tissue can be determined at nanometer scale. Raw ultrasound data, containing the amplitude as well as the phase information is required for this analysis. A 2D coarse-to-fine strain estimation strategy is proposed to calculate the minute differential displacements in tissue, while the tissue itself is moving on a macro scale.

The technique was validated using phantom experiments. These experiments demonstrated that accurate strain images can be determined using the proposed technique. Cardiac evaluation in dogs showed that the strain can be determined in three dimensions. The strain curves over the cardiac cycle are in correspondence with the severity of the stenosis of the aortic valve.

In patients with a reconstructed cleft lip, the orbicular oral muscle in the reconstructed region showed decreased strain values. In normal individuals, similar strain values were found for all regions of the muscle.

Ultrasound strain imaging is a promising technique enabling the addition of functional information to the geometrical information that is already provided by the conventional ultrasound imaging technique.

Index Terms— ultrasound, strain imaging, elastography, cardiac function, cleft lip, surgical reconstruction.

1. INTRODUCTION

Ultrasound strain imaging of tissues using ultrasound is becoming an important tool for diagnosis. In contrary to the conventional approach in which geometrical information is assessed, strain imaging provides information on the function of the tissues.

Ultrasound strain imaging or elastography was first described in 1991 by Ophir and colleagues [1]. Although in the first 10 years this technique was mainly used for tumor detection, a tendency towards cardiac, vascular and muscular applications can be observed over the last five years [2-4]. Elastography is based on acquiring multiple images of tissue while it is deforming. As an initial step, the displacement along the ultrasound scan lines is estimated. In ultrasound imaging, time and space are related to each other by assuming a constant speed of sound. Normally, the speed of sound in human tissues is around 1540 m/s. In case, the displacements of interest might are in the sub-micrometer range, the time delay between the signals is in the order of nanoseconds. It is obvious, that these displacements can not be determined from the conventional echograms that have typically a resolution of 200 to 500 micrometer, depending on the ultrasound frequency used. In making an echogram, only the amplitude information of the ultrasound signals is used. However, by using also the phase information of the ultrasound signals, smaller displacements can be assessed. An ultrasound machine normally does not provide the wanted, so-called “raw” ultrasound or radio frequency (rf) data. For this purpose, it needs to be equipped with an rf-interface.

Especially for fast moving structures like the heart and muscles, temporal resolution is an important issue: to properly track the tissue while it is contracting, 50 to 100 images per second are required. In contrast to most other diagnostic techniques, ultrasound offers this temporal resolution. In this study, we focus on functional imaging of the heart and muscles.

Cardiac strain imaging has been assessed as a non-invasive technique for mapping the mechanical properties of myocardial tissue and monitoring cardiac diseases, such as hypertrophy [3]. After the introduction of real-time 3D ultrasound imaging techniques the development and research of 3D strain estimation has been triggered. Full 3D cardiac imaging is preferred over 2D techniques considering the magnitude and complexity of the 3D motion and deformation of the heart. Moreover, the anisotropic mechanical properties of muscle tissue prevent proper classification of tissue elasticity using 1D or 2D strain imaging techniques.

Similar techniques as used for cardiac applications are used for deformation and strain imaging of muscles. We are developing the technique for monitoring muscle function in patients with neuromuscular diseases, and for evaluation of the surgical reconstruction of cleft lips. One out of 500 to 1000 babies is born with a facial cleft. Cleft lip, with or without cleft palate, is the most common of these facial clefts. Reconstruction of the upper lip and the restoration of the continuity of circular muscle in the lip (orbicular oral muscle) is an important step in the treatment of these children. However, a surgical intervention leads inevitably to scar formation. The amount of scar tissue and its position both have functional and esthetic consequences [5]. The esthetic outcome of an intervention may be visually judged, but it remains unclear whether the continuity and functionality of the muscle have been established. Ultrasound strain imaging might be a useful tool to identify the function of the orbicular oral muscle..

2. MATERIALS AND METHODS

2.1 Materials

For all phantom and in vivo studies, raw ultrasound data were acquired with a Philips SONOS 7500 real-time 3D system equipped with an RF-interface. Cardiac data was acquired using a 4 MHz, 3D matrix array transducer (X4) and sampled at 19.5 MHz. Muscle data was acquired with a 7 MHz linear array transducer (11-3L) at a sampling rate of 39 MHz. All data was first stored internally in the ultrasound machine and then transported to a workstation for off-line processing.

For experimental verification, a phantom was made of 8.0 % gelatine (1.0 % agar) with a hard cylindrical inclusion (3.0 % agar, approximately four times stiffer). The phantom (10 cm x 10 cm x 10 cm) was compressed with a large plate compressor by applying a stepwise displacement of 5.0 mm (leading up to a total of 10.0 % strain in 20 steps).

Cardiac strain imaging was evaluated using a pilot animal study in which dogs (n=2) with an induced valvular aortic stenosis are being monitored in time. The valvular aortic stenosis results in a chronic pressure overload of the left ventricle leading to hypertrophy (and eventually fibrosis) of the myocardial tissue. Using ECG-triggered BiPlane imaging, frame-to-frame deformations were obtained over the heart-cycle for a manually segmented region-of-interest (ROI) of the lateral wall in both the short-axis (Sax) and long-axis (Lax) planes.

Muscular strain imaging was evaluated using acquisitions in normals (n=3) and in patients with a reconstructed cleft lip (n=3). The upper lip of the subjects was prepared by extruding approximately a one-centimeter layer of commercial ultrasound contact gel (Kendall Meditec, Mirandola (MO), Italy) over the full width of the upper lip in transversal scanning. Then the transducer was carefully applied to this layer while avoiding inclusion of air bubbles between transducer surface and gel. During the acquisition, the subject was asked to slowly contract the lips by making a “kissing movement”. This movement is caused by contraction of the orbicular oral muscle, which is located in the upper and lower lips as a circular structure. If this circular muscle is interrupted by scar tissue, this scar tissue will only passively deform.

2.2 Data processing

An iterative 2D correlation-based strain algorithm was implemented. Displacements were estimated using RF-signals in the axial direction (∂ax) and the demodulated data in the lateral direction (∂lat). To obtain sub-sample and sub-line resolution, interpolation of the data is required. Therefore, a sub-line resolution of 1/100th line requires the interpolation of 100 rf-lines in between the measured lines, which is a time consuming process. However, if a parabolic shape of the peak of the cross-correlation function (CCF) is assumed, the displacement in both directions (∂ax and ∂lat) can be determined by solving analytical expressions [6]. Using this approach, time delays between signals as small as 1 nanosecond can be determined corresponding with a displacement estimate of 200 nanometer. To improve the strain estimates, spatial registration and local stretching of the data was applied to reduce decorrelation effects. To increase elastographic resolution, the window size was decreased using previous (interpolated) estimates as offset values (coarse-to-fine). A small 5 x 5 median filter was applied to remove outliers in the displacement images. Both axial and lateral strain images were obtained using a least squares strain estimator [6]. Lateral strain values were smoothed using a 5 x 21 averaging filter.

For cardiac applications, semi three-dimensional strain was obtained by using a BiPlane imaging mode. In this mode, ultrasound data in two orthogonal planes is acquired. Analysis of the data results in an axial and lateral strain image for one plane and in axial and elevational strain image for the other plane.

3. RESULTS

3.1 Phantom experiment

The developed strain algorithms were validated using the phantom. The cumulative strain images of the gelatin

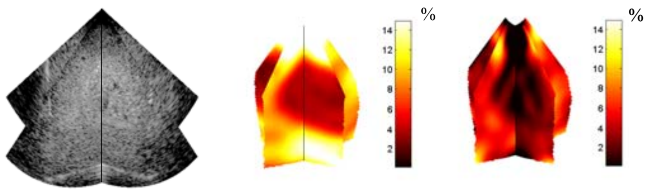

Figure 1. a) BiPlane image of the gelatin phantom; b) Axial cumulative BiPlane strain image; c) Lateral cumulative BiPlane strain image.

phantom are shown in Fig. 1. This BiPlane data shows high strain in the soft background and lower strain values in the hard inclusion. The axial and lateral strains were displayed after correcting the measured displacements for the angle between the measured lines and the axis of the transducer.

The axial strain images show better contrast between inclusion and background than the lateral strain images. This is caused by the fact that for axial strain estimation the phase information is available, in contrary to the lateral direction.

3.2 Cardiac strain imaging

Cardiac strain was evaluated in two dogs 6 months after creating a valvar aortic stenosis. Biplane images were acquired in a dog with a pressure gradient over the valve of ΔP = 100 mmHg. The measured cumulative mean radial (i.e. 'axial') strain in the ROI reveals a maximum strain up to 50% (Fig. 2). A drift in the strain values was removed by applying a linear trend correction algorithm. The radial strain curves for both planes (S_{ax} and L_{ax}) were calculated independently of each other, but appeared to be almost identical. The maximum circumferential and longitudinal cumulative mean strain are considerably lower (-20%). However, the shape is similar to the radial strain curves.

The second dog with a higher gradient over the valve (ΔP = 200 mmHg) reveals a lower maximum radial strain (40 %) and a plateau is observed in the radial strains, which is also clearly visible in the circumferential and longitudinal strain curves (Fig. 2). This phenomenon was observed in a previous study in humans with a valvular aortic stenosis [7]. The high pressure gradient and the observed thickness of the heart muscle confirm the suspected hypertrophy but a pathological analysis of the heart tissue will be necessary.

3.3 Muscle strain imaging

The cumulative strain images acquired in a representative normal volunteer over the full cycle show positive strain values in the orbicular oral muscle from initial resting state to kissing condition and strain values returning to zero after release of the pout condition and going back to initial state. This corresponds to thickening of the muscle. The axial strain images were quantified by selecting regions in the orbicular oral muscle. In normal lips, similar deformation patterns in the left, middle and right part of the muscle were observed with a maximum axial strain of 20%.

In patients, strain patterns different from the normal strain patterns could be observed. Depending on the rate of success of the surgical procedure, small to large deviations were observed. In all regions with scar tissues decreased strain values were found. In a patient with severe disability, a maximum strain value of 5% was found in the scar tissue region. In a patient with a reconstructed cleft lip, decreased strain values (up to 12 % strain) were found in the scar tissue region, however, the regions was rather small. The observed strain curves might be enhanced further by tracking the region-of-interest in time during the contraction cycle.

4. DISCUSSION AND CONCLUSION

Ultrasound strain imaging is a technique to assess tissue displacements in the order of 200 nanometers. Using these displacement estimates as an input for the strain algorithm, tissue deformation can be assessed. Phantom experiments reveal that accurate strain information can be determined, corresponding to the geometry of the phantom. Due to the lack of phase information in the direction perpendicular to the ultrasound lines, poorer quality of the strain images is obtained in this direction.

Cardiac evaluation demonstrates that 3D strain imaging of this fast contracting organ is feasible. Since the strain is

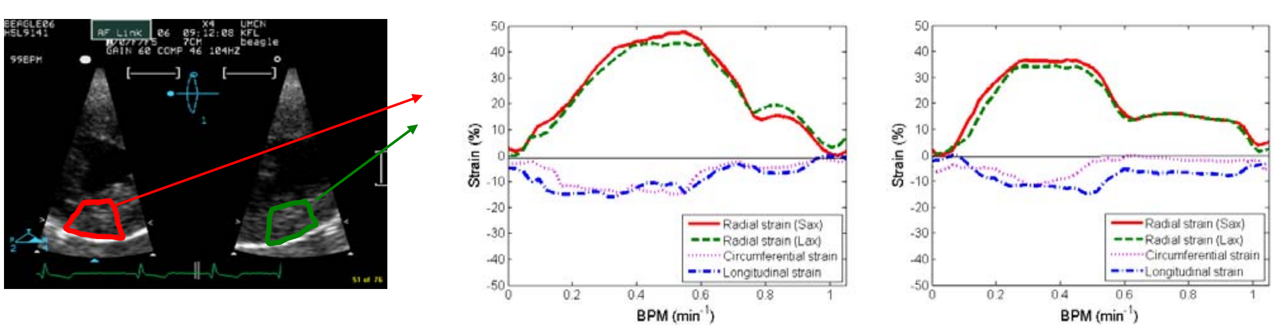

Figure 2. a) BiPlane images of the lateral wall with the used ROI's (red/green line); b) Mean cumulative strains for the beagle with ΔP = 100 mmHg and c) mean cumulative strains of the beagle with ΔP = 200 mmHg during one heart cycle.

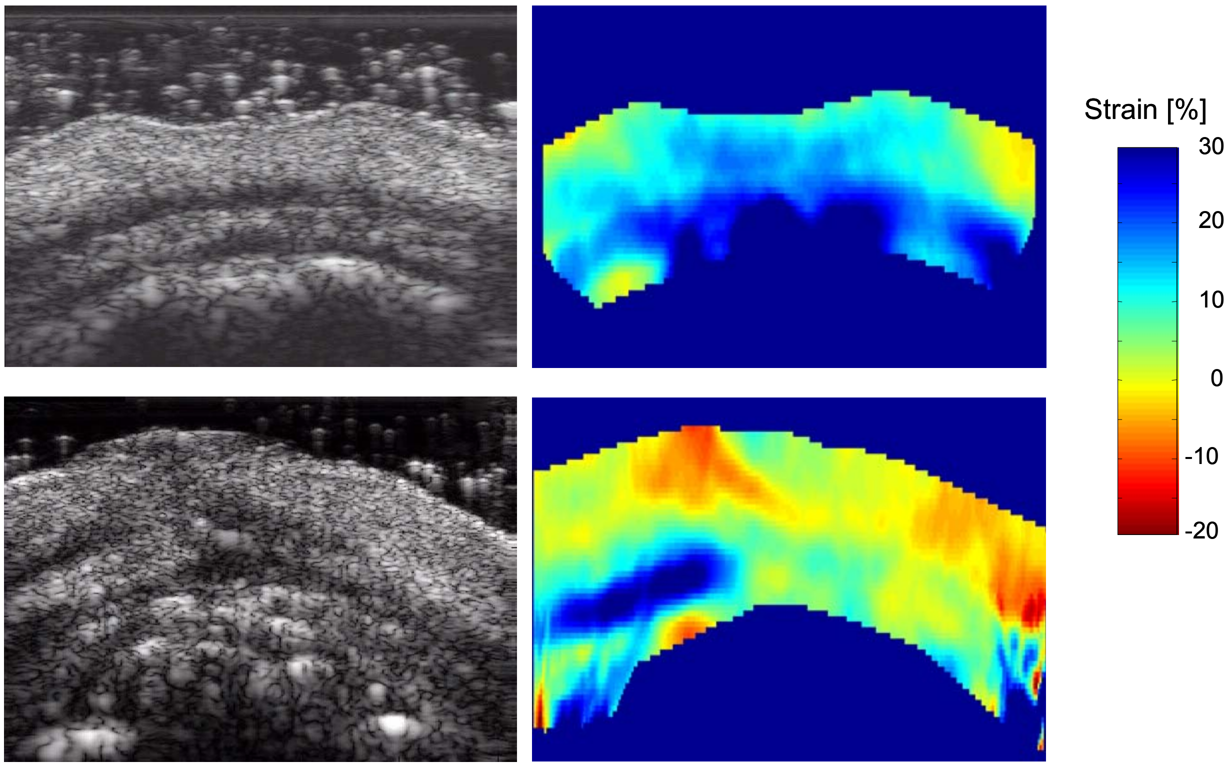

Figure 3. Echograms (left column) and strain images (right column) of a normal individual (top row) and a patient with a reconstructed cleft lip (bottom row). The strain images show similar deformation in all regions in the normal individual whereas lack of deformation is observed in the patient repaired cleft.

obtained in a relatively small region, local function of the heart can be obtained. The pilot experiments in the animal model yielded particular strain curves over the cardiac cycle that were also obtained in patients with a similar disease. The availability of histological data might reveal a direct relation between the function of the heart muscle as assessed with ultrasound strain imaging and the composition. Especially in children with a congenital heart disease, this information might prevent heart failure. Currently, children with a congenital valvar aortic stenosis are treated based on the pressure gradient over the valve. Direct information on the heart muscle function might turn out to be a better suited parameter.

Ultrasound strain imaging of the upper lip reveals differences between normal individuals and patients with a reconstructed cleft lip. The strain images show the regions with muscle malfunction and also provide quantitative information on the remaining functionality. Currently, the outcome of the intervention is evaluated using standardized photos. It is clear that this technique only provides information on the external esthetics, and that direct insight in the orbicular oral muscle as obtained with strain imaging might improve diagnosis.

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